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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|-----------------------|---------------------|------------------|
| 10/719,571 | 11/20/2003 | Volker Schellenberger | GC560-DI-C1 | 3420 |
| 7590 | 11/17/2005 | | EXAMINER | |
| Genencor International, Inc. 925 Page Mill Road Palo Alto, CA 94034-1013 | | | MARVICH, MARIA | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1633 | |

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|-----------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/719,571 | SCHELLENBERGER ET AL. | |
| | Examiner | Art Unit | |
| | Maria B. Marvich, PhD | 1633 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 22 August 2005.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 49,51-54 and 56-71 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) 49, 51-54 and 56-70 is/are allowed.

6) Claim(s) 71 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 20 November 2003 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

This office action is in response to an amendment filed 8/22/05. Claims 1-48, 50 and 55 have been canceled. Claims 51, 61 and 71 have been amended. Claims 49-54 and 56-71 are pending.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are no new grounds of rejection herein and therefore, this action is final.

Receipt of a terminal disclaimer in the amendment filed 8/22/05 is acknowledged. It is noted that the double patenting rejection in the office action filed 3/24/05 incorrectly refers to the US patent as 6,705,503. However, the terminal disclaimer correctly identifies the patent as US 6,706,503.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 71 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 71 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in the office action mailed 3/24/05 and restated below. The rejection has been reworded based upon applicants' amendment.**

The instant invention recites a method of producing a heterologous protein with a microorganism comprising a heterologous mutator gene comprises *mutD* mutations or homologues thereof.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

Applicants' invention is drawn to a method of producing a protein from an evolved microorganism comprising obtaining a microorganism that comprises a heterologous mutator gene. In claim 71, applicants recite that this mutator gene can be *mutD* mutations or homologues thereof. Although the instant claims are directed to methods, adequate description of the methods first requires an adequate description of the materials, which provide the means for practicing the invention. The Guidelines for Written Description state "The claimed invention

as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art".

The specification discloses that a mutator gene is a DNA repair gene with a mutation. DNA repair genes disclosed in the specification include *mutD*, *mutT*, *mutY*, *mutM*, *mutH*, *mutL*, *mutS* and *mutU*. For example, *mutD* is the epsilon subunit of DNA polymerase III comprising mutations that impair proofreading function (see e.g. page 7, line 6-25). Specifically, applicants generate sixteen *mutD* mutations (see table 1). These plasmids are used to transform target organism and are further exposed to conditions that generate evolved microorganisms. With the exception of the nucleic acid and amino acid sequences for *mutD*. However, applicants do not disclose any homologs, which are defined as functionally related DNA repair gene (page 7, line 16). Furthermore, the specification does not disclose any of the sequences of the recited genes nor provide a description of the genes such that the structural requirements of the genes can be envisioned. Neither the prior art nor the specification has provided adequate written description to support or illustrate the genus encompassed by the claim. Therefore, applicants have not clearly identified the genus of *mutD* homologues. Given the absence of disclosed or art recognized correlations between structure and function of homologues of *mutD* genes, the large number of potential homologues that can be generated in said genes and the uncertainty that any homologue will be functional, it must be considered that any homologue must be empirically determined. By disclosing *mutD* mutations, the applicants have not reduced to practice homologues of *mutD* mutations. Given the diversity of the recited mutator genes, the absence of disclosed or art recognized structure-function relationships and the unpredictability of the art, the

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disclosure of one example in one genus would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 112, first paragraph on page 10 of the amendment filed 8/22/05. Applicants argue that the claim have been amended to recite *mutD* mutations or homologues, which according to applicant are supported by the specification.

Applicants' arguments filed 8/22/05 have been fully considered but they are not persuasive. Applicants have recited a large genus of mutator genes by recitation of homologues of *mutD* mutations. Applicants have generated mutations in a single gene, termed *mutD* and have disclosed several of these mutations which are functional in the method to produce heterologous proteins. However, applicants have not disclosed any homologues of these genes. The specification lacks any guidance as to the structural requirements of the genes that can provide heterologous mutator function. Therefore, the specification has failed to describe the genes such that the nexus of structure and function is apparent. Given the lack of disclosure as to the structural requirements of the recited mutator genes and the lack of disclosure as to homologues, the skilled artisan cannot envision the detailed structure of the broad class of homologues, functionally related genes, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that the sequence is part of the invention and a reference to a potential method for isolating it.

Conclusion

Claim 71 is rejected.

Claims 49-54 and 56-70 are allowed.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

November 10, 2005


DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER